functionality or decreased functionality.

To design functionally equivalent polypeptides, it is useful to distinguish between conserved positions and variable positions. This can be done by aligning the amino acid sequences of GLUTX that are obtained from various organisms or by aligning GLUTX with other identified glucose transporters, *e.g.*, GLUT1 (SEQ ID NO:3), GLUT2 (SEQ ID NO:4), GLUT3 (SEQ ID NO:5), GLUT4 (SEQ ID NO:6), and GLUT5 (SEQ ID NO:7), shown in Fig. 3). Skilled artisans will recognize that conserved amino acid residues are more likely to be necessary for preservation of function. Thus, it is preferable that conserved residues are not altered. Alignment of GLUTX with other glucose receptors will reveal regions that are more highly conserved. Such regions are preferably not altered.

Mutations within the GLUTX coding sequence can be made to generate variant GLUTX genes that are better suited for expression in a selected host cell. For example, N-linked glycosylation sites can be altered or eliminated to achieve, for example, expression of a homogeneous product that is more easily recovered and purified from yeast hosts which are known to hyperglycosylate N-linked sites. To this end, a variety of amino acid substitutions at one or both of the first or third amino acid positions of any one or more of the glycosylation recognition sequences which occur (in N-X-S or N-X--), and/or an amino acid deletion at the second position of any one or more of such recognition sequences, will prevent glycosylation at the modified tripeptide sequence (see, *e.g.*, Miyajima *et al.*, *EMBO J.* 5:1193, 1986).

The polypeptides of the invention can be expressed fused to another polypeptide, for example, a marker polypeptide or fusion partner. For example, the polypeptide can be fused to a hexa-histidine tag to facilitate

purification of bacterially expressed protein or a hemagglutinin tag to facilitate purification of protein expressed in eukaryotic cells. In addition, a GLUTX polypeptide can be fused to GST.

The polypeptides of the invention can be chemically synthesized (*e.g.*, see Creighton, "Proteins: Structures and Molecular Principles," W.H. Freeman & Co., NY, 1983), or, perhaps more advantageously, produced by recombinant DNA technology as described herein. For additional guidance, persons of ordinary skill in the art may consult Ausubel *et al.* (*supra*), Sambrook *et al.* ("Molecular Cloning, A Laboratory Manual," Cold Spring Harbor Press, Cold Spring Harbor, NY, 1989), and, particularly for examples of chemical synthesis, Gait ("Oligonucleotide Synthesis," IRL Press, Oxford, 1984).

III. Transgenic animals

GLUTX polypeptides can also be expressed in transgenic animals. Such transgenic animals represent model systems for the study of disorders that are either caused by or exacerbated by misexpression of GLUTX, or disorders that can be treated by altering the expression of GLUTX or the activity of GLUTX (even though the expression or activity is not detectably abnormal). Transgenic animals can also be used for the development of therapeutic agents that modulate the expression of GLUTX or the activity of GLUTX.

Transgenic animals can be farm animals (*e.g.*, pigs, goats, sheep, cows, horses, rabbits, and the like) rodents (such as rats, guinea pigs, and mice), non-human primates (*e.g.*, baboons, monkeys, and chimpanzees), and domestic animals (*e.g.*, dogs and cats). Transgenic mice are especially preferred.

Any technique known in the art can be used to

introduce a GLUTX transgene into animals to produce founder lines of transgenic animals. Such techniques include, but are not limited to, pronuclear microinjection (U.S. Pat. No. 4,873,191); retrovirus mediated gene transfer into germ lines (Van der Putten *et al.*, *Proc. Natl. Acad. Sci., USA* 82:6148, 1985); gene targeting into embryonic stem cells (Thompson *et al.*, *Cell* 56:313, 1989); and electroporation of embryos (Lo, *Mol. Cell. Biol.* 3:1803, 1983).

The present invention provides for transgenic animals that carry a GLUTX transgene in all of their cells, as well as animals that carry a transgene in some, but not all of their cells. For example, the invention provides for mosaic animals. The GLUTX transgene can be integrated as a single transgene or in concatamers, for example, head-to-head tandems or head-to-tail tandems. The transgene can also be selectively introduced into, and activated in, a particular cell type (Lasko *et al.*, *Proc. Natl. Acad. Sci. USA* 89:6232, 1992). The regulatory sequences required for such a cell-type specific activation will depend upon the particular cell type of interest, and will be apparent to those of skill in the art.

When it is desired that a GLUTX transgene be integrated into the chromosomal site of an endogenous GLUTX gene, gene targeting is preferred. Briefly, when such a technique is to be used, vectors containing some nucleotide sequences homologous to an endogenous GLUTX gene are designed for the purpose of integrating, via homologous recombination with chromosomal sequences, into and disrupting the function of the nucleotide sequence of the endogenous gene. The transgene also can be selectively introduced into a particular cell type, thus inactivating the endogenous GLUTX gene in only that cell type (Gu *et al.*, *Science* 265:103, 1984). The regulatory sequences required